the present case and there was no evidence of congestive failure.

Ankle edema has been previously noted in P. vivax malaria and has been ascribed to the low serum albumin that is often observed.[2] The latter is a result of changes in the reticuloendothelial system, primarily in the liver, which together with the increased globulin account for the abnormalities in results of liver flocculation tests.[6]

Finally, albuminuria, cylindruria and microscopic hematuria and pyuria may be due to the alterations reported pathologically in the renal glomeruli and tubules.[1] These are not common in P. vivax malaria and when present are transient, mild and reversible. Renal disease varying from that typical of nephrosis, seen mainly with P. malariae malaria, to renal failure secondary to hemoglobinuria due to P. falciparium malaria, has also been reported.[3, 8]

SUMMARY

An unusual case of P. vivax malaria, with anemia, cardiomegaly, ankle edema, hepatomegaly and renal involvement, has been reported. The mechanisms have been discussed.

2515 South Highland Avenue, Los Angeles.

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Falciparum Malaria

Report of a Fatal Case and Autopsy Findings

EDWARD E. HARNAGEL, *M.D.*, and
FLORENCE V. RHUDY, *M.D.*, Los Angeles

MALARIA, although considered to be one of "humanity's chief scourges"[2] is an uncommon disease in the civilian populace of California. In Los Angeles County, for example, the median incidence of this disease in a five-year period (1948-1952) was one case per year.[4] In most of these cases the causative organism was plasmodium vivax. Malaria due to P. falciparum is rare; in all California only one case in 1953 and only two in 1952 (one of which was listed as "probable") were reported to the Bureau of Acute Communicable Diseases.[7] Moreover, symptomatic responses to falciparum malaria are much less distinctive than those to vivax or quartan infections and frequently offer little help in reaching a presumptive diagnosis. A disease that is rare and without distinctive features presents a formidable diagnostic problem. In the case here presented the disease was successively presumed to be influenza, intestinal obstruction and acute cholecystitis before a correct diagnosis was made on the basis of observation by an alert laboratory technician.

REPORT OF A CASE

A 65-year-old woman had fever, lassitude, generalized arthralgia and myalgia of three days' duration. Chilly sensations had been present at the onset, for a few hours only. The patient had returned from a vacation in Mexico only a few days before becoming ill. On questioning she said that she had been in a region where malaria is endemic but that rainfall had been unusually light and there had been no mosquitoes about.

The body temperature was 101 degrees F. A provisional diagnosis of influenza was made and symptomatic therapy was prescribed. The patient was not improved the following day, and since she lived alone she was admitted to the hospital for care. The body temperature at the time of admittance was 99.4 degrees F., the pulse rate was 70, respirations were 22 per minute and the blood pressure was 146/88 mm. of mercury. There was slight tenderness in the right upper quadrant of the abdomen and very slight abdominal distention.

On the second hospital day, the patient awoke very nauseated and vomited a small amount of clear fluid containing brownish flecks which by chemical test were found to contain blood. She also complained of severe abdominal pain; and an increase in abdominal distention and some diffuse abdominal tenderness was noted. The body temperature was subnormal most of this day. Because of the many stab cells and diminished number of platelets noted on examination of the blood the day of admittance, the pathologist requested additional specimens (see Appendix A—additional laboratory data). These were taken on the third hospital day but revealed nothing diagnostic. Abdominal pain and distention continued and the patient was not able to retain even liquids by mouth. The possibility of intestinal obstruction was considered. A plain film of the abdomen showed a large amount of gas in the large bowel and also in the right upper quadrant a pyriform shadow of increased density, which was con-

sidered to be the gall bladder. In view of the pronounced distention of the colon, a barium enema was given but as no obstructive lesion was demonstrated it was concluded that the distention might be owing to ileus.

During the fourth and fifth hospital days the temperature fluctuated between 96.8 degrees F. and 102.4 degrees F.; the abdominal symptoms and signs persisted. Shortly after midnight of the sixth hospital day the patient, awakened by severe epigastric pain, became nauseated and vomited several mouthfuls of brownish, mucoid liquid. The blood pressure at that time was 78/50 mm. of mercury. The patient was quite apprehensive and dyspneic and the rate of respirations was 36 per minute. The abdomen was more distended. Peristaltic sounds were hyperactive and there was definite tenderness in the right upper quadrant of the abdomen. A surgical consultant who examined the patient at this time was able to outline a mass in the right upper quadrant which he believed was an acutely inflamed gall bladder surrounded by omentum. He felt that the patient had acute cholecystitis, but in view of the duration of the process recommended conservative management. During this day, the temperature rose to 102.6 degrees F. The patient appeared restless but quite weak. The abdominal symptoms continued.

A laboratory technician, examining a specimen of blood on the sixth day for a routine determination of the numbers of cells, observed numerous malaria parasites. Upon further study they were observed to be predominantly multiple ring form trophozoites with occasional shizont forms and infrequent crescent-shaped gametocytes typical of plasmodium falciparum. Administration of quinacrine, 0.2 gm. every six hours, was started on the seventh day and a total of 0.8 gm. was given. The patient was able to retain this medication but on this day she had a chill with a rise in temperature to 101.6 degrees F., and there was no decrease in the number of parasites observed in a specimen of blood.

On the eighth day the patient became very dyspneic and had some bronchial wheezing and audible rales at both lung bases. The temperature reached 103.2 degrees F. Icterus was noted for the first time and also a large area of ecchymosis in the lumbar region was observed. A total of 3 gm. of chloroquine was given on the eighth and ninth days, of which the patient retained approximately 2 gm. During the ninth day icterus became more intense and for the first time the patient was somnolent, although easily aroused, and even though obviously gravely ill, she was rational and oriented. The temperature during the ninth day fluctuated between 99.0 degrees F. and 101.8 degrees F. However, the output of urine dropped precipitously to 565 cc., despite an intake of liquids of 2900 cc. Several specimens of urine were deep brown in color and thick in consistency. Two smears of specimens of blood taken about twelve hours apart on this day revealed the parasites were still numerous. Quinine dihydrochloride, 3 gm. intravenously, was given on the ninth and tenth days. On the morning of the tenth day rather profuse epistaxis occurred. Respirations were 16 per minute with the patient at rest, but upon very slight exertion rose to 24 to 28 per minute. The maximum temperature during this day was 101.0 degrees F. The urinary output increased to 820 cc. in 18 hours, and the urine was not so dark as on the previous day. Basal rales and infraorbital and pretibial edema were noted. In the evening the patient was rather comfortable and appeared somewhat improved over the previous day. However, at 11 p.m. a Jacksonian seizure involving the left hand and left leg occurred. It was rapidly followed by generalized convulsion and the patient died.

AUTOPSY

Macroscopic: There was pronounced jaundice of the skin and sclerae. Each of the pleural cavities and the peritoneal cavity contained approximately 500 cc. of yellowish-pink serous fluid. The lungs were moderately congested with frothy reddish-yellow fluid pouring freely from the opened bronchi. There was obvious splenomegaly and hepatomegaly. The spleen, which weighed 350 gm., showed a soft, mushy, dark reddish-purple pulp in which the malpighian corpuscles were not discernible. The liver, which weighed 2,250 gm., had finely mottled, reddish to yellowish-brown cut surfaces of soft consistency. The gall bladder was normal. There was generalized enlargement of lymph nodes, involving particularly the periaortic and mesenteric lymph nodes, which were firm and on cut surfaces were mottled reddish to pinkish-gray. There were a few petechial hemorrhages on the mucosal and serosal surfaces of the stomach and duodenum. The brain substance was slightly edematous and had a faintly yellow cut surface. There were no demonstrable petechiae. The vessels of the leptomeninges appeared slightly congested. The iliac bone marrow was dark reddish-gray. In the remainder of the organs no significant gross abnormalities other than moderate congestion were noted.

Microscopic: Conspicuous changes, chiefly in the liver, spleen and kidneys, were observed.

In the spleen there was loss of normal histological architecture with marked vascular congestion of the sinusoids. The latter were filled with hemolyzed red cells, large mononuclear cells and macrophages laden with yellowish-brown pigment granules and nuclear debris. A few parasitized red cells were demonstrable.

There was evidence in the liver of pronounced parenchymatous degeneration with vacuolization and cloudy swelling of the hepatic cells. The sinusoids were dilated and filled with numerous small round cells, pigment-laden macrophages and parasitized red cells.

In the kidneys moderate parenchymatous degeneration of the tubular epithelium was noted. The tubules contained yellowish-pink granular casts. Similar amorphous pink-staining granular material

was also present in the subcapsular spaces of the glomeruli which were otherwise not remarkable.

There was minimal glial and perivascular edema throughout the cerebral cortex. Parasitized red cells were demonstrable in the capillaries and larger vessels. In addition, there were scattered pigment-laden macrophages throughout the glial substance.

There was moderate vascular congestion in the lungs, with parasitized red cells demonstrable in the capillary lumina.

Upon examination of sections from the iliac crest, hyperplastic marrow with an increase of erythroid and myeloid elements was noted. Parasitized red cells and pigment-laden macrophages were numerous and abundant.

DISCUSSION

Malarial infections have a predilection for organs of the reticuloendothelial system, namely, the liver, spleen, bone marrow and lymph nodes.[1] When macrophages of these organs fail to localize the infection, parenchymatous degeneration may take place in several organs. This is due either to the rapid blood destruction and anemia, or to thrombosis of capillaries, apparently occurring as a result of the agglutination of parasitized erythrocytes.[6] Although such cells were widespread in the vascular spaces of virtually all tissues examined in the present case, thromboses were not seen, possibly owing to the decreased prothrombin content and thrombocytopenia. Hence, it was assumed that the parenchymal damage noted particularly in the liver and kidneys was related to anoxia resulting from hemolysis and anemia.

Covel[3] recently wrote: "There is no known disease which may simulate as many other ailments as falciparum malaria. . . ." Since the experience with the case reported herein, however, the authors have learned that the clinical features observed in the patient—high, irregular fever, nausea, vomiting, abdominal pain and distention, jaundice and epistaxis—are quite characteristic of a type of falciparum malaria well known to malariologists as "bilious remittent fever."[5, 8, 9] Unfamiliarity with this syndrome and consequently the delay in making the correct diagnosis, as well as the age of the patient, the type of infection and the resistance to substantial doses of three anti-malarial drugs were all contributing factors to the fatal outcome.

SUMMARY

A fatal case of "bilious remittent fever" type of P. falciparum infection is presented. It was successively presumed to be influenza, intestinal obstruction and finally cholecystitis before a correct diagnosis was established.

511 So. Bonnie Brae.

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APPENDIX "A"—ADDITIONAL LABORATORY DATA

First day: Hemoglobin, 14.1 gm. per 100 cc.; erythrocytes, 4,430,000 per cu. mm.; leukocytes, 4,400 per cu. mm. with 85 per cent polymorphonuclear cells (76 non-filamented, 9 filamented), and 15 per cent lymphocytes; platelets, fewer than normal. Results of urinalysis were within normal limits except for mild pyuria. No abnormality seen in x-ray film of chest.

Third day: Erythrocytes, 4,700,000 per cu. mm.; leukocytes, 5,000 per cu. mm.—80 per cent polymorphonuclear cells (33 non-filamented, 47 filamented), and 20 per cent lymphocytes; platelets, 85,000 per cu. mm.

Fifth day: Result of test for occult blood in stool, positive.

Sixth day: Serum amylase, 35 units per 100 cc. (normal 40—110 units); serum lipase, 100 units (normal 85—205 units); hemoglobin, 12.9 gm. per 100 cc.; erythrocytes, 3,820,000 per cu. mm.; leukocytes, 6,100 per cu. mm.—83 per cent polymorphonuclear cells (45 non-filamented, 38 filamented), 16 per cent lymphocytes and 1 per cent monocytes. An electrocardiogram indicated left ventricular strain.

Eighth day: Erythrocytes, 2,930,000 per cu. mm.; platelets, 58,000 per cu. mm. Prothrombin: Patient's time, 38 seconds; control, 16 seconds; prothrombin content, 16 per cent. Serum bilirubin, 5.4 mg. per 100 cc. direct and 0.7 mg. indirect.

Ninth day: CO_2 combining power, 23 volumes per cent. Prothrombin: Patient's time, 27 seconds; control, 15 seconds; prothrombin content, 26 per cent. Whole blood chlorides, 516 mg. per 100 cc.

Tenth day: Prothrombin: Patient's time, 19 seconds; control, 15 seconds; prothrombin content, 60 per cent. Erythrocytes, 3,120,000 per cu. mm.; hemoglobin, 10.0 gm. per 100 cc.; leukocytes, 8,000 per cu. mm.—77 per cent polymorphonuclear cells (38 non-filamented, 39 filamented) and 23 per cent lymphocytes.